

## **Proteomics: The Challenge of Proteomics for Cancer (Part 2 of 3)**

**Balintfy:** In part one of this three part series, on proteomics, the study of proteins, we learned how proteins are the workhorses of DNA, the genetic make-up or blueprints that make us who we are. In this part two, we continue our talk with Dr. Henry Rodriguez, the director of the Clinical Proteomic Technologies for Cancer programs at the NCI. We discuss the challenges of proteomics as a tool for early detection of cancer. First, Dr. Rodriguez, welcome back.

**Dr. Rodriguez:** Thank you.

**Balintfy:** What are some of the challenges of studying cancer proteins and expanding the number of cancers that can be identified through testing for protein biomarkers?

**Dr. Rodriguez:** I think the key message here is what we have is the lack of well-characterized different platforms, either for the discovery or the verification of different protein markers coupled with the lack of various performance standards, metric software, necessary reagents and, of course, biospecimen collection protocols, or standard operating procedures, that ultimately can be used across multiple institutions or laboratories. And this ultimately seems now to limit the number of cancer protein or biomarker tests that eventually become available to the general public.

**Balintfy:** Metrics is something we use here at the NIH a lot, but maybe the general public doesn't really know what we mean when we're talking about metrics or measurement and how that would make a difference in validating the science. Can you touch on that a little bit?

**Dr. Rodriguez:** Yeah, so what becomes quite important is when one laboratory actually does experiments, if you really want to test a robust list and actually look at what you're measuring, it becomes very important to have multiple institutions to be able to reproduce that for you. Well, the way that's typically is going to be done is you need to come across your network and say, "Let's develop standard ways of doing this so you can have the assurance that what we're measuring in one laboratory is not going to be attributed to the way that laboratory happens to have done it." To make it very robust, when we have assurance of what we're looking at and it's valid from a biological perspective—it's not going to be attributed to bias—multiple institutions should have that ability to measure that same animal and come up with those same conclusions.

**Balintfy:** Maybe this is an oversimplification, but I would think of it as, you know, you can have one recipe in one kitchen, and it should turn out the same as the recipe in the other kitchen.

**Dr. Rodriguez:** Right, so and if you use that in an analogy, technically you have different cooks at each one of these kitchens, but the question becomes just how good is the oven that we're using? Just how good is that recipe we're using? Because if you begin to cook and develop the same cake at the end, then that tells you that what you're developing, all that is going to be very robust.

**Balintfy:** Great. Are there some problems associated with those making sure that those laboratories and the matrixes are consistent?

**Dr. Rodriguez:** You know, one way of looking at it is you can kind of look at the challenges that exist when it comes to this field. If you simply look at the scientific literature today, what's remarkable is now there's over a thousand. Let me say that again. There's over 1,000 cancer protein biomarker candidates that have been identified by the research community over the past 10 years at least. And this list continues to grow on a daily basis. Now, the challenge is that very few of these protein biomarker candidates ultimately make their way into a clinical setting. Part of the reason is that today, laboratories across the country and around the world collect, store, and they study proteins in different ways.

**Balintfy:** So what are some advances you think are necessary to resolve these problems?

**Dr. Rodriguez:** So current and emerging protein measurement technologies, they really need to be optimized and calibrated through the use of standards, ultimately to produce comparable results between these laboratories that I've alluded to. At the same time, high quality reagents are going to be needed.

**Balintfy:** So what exactly is a reagent?

**Dr. Rodriguez:** A reagent happens to be a physical material that you use that you will run through your instrument to make sure that it's working correctly.

**Balintfy:** So that's just one of the resolutions that's needed, and there are others as well in terms of technology?

**Dr. Rodriguez:** Yeah, exactly. So I think one of the good things about NCI is that through the Clinical Proteomics Technologies for Cancer, it actually developed as a very elaborate network. That network is actually looking at the existing platforms that are today. But the other thing we have to ask the question, are the technologies we have today going to be the ones that are going to be required let's say five, 10 years from now? So I think you should always be looking at, can we develop better tools, both from a hardware perspective and a software perspective, to mine the vast amounts of data that's being generated.

But I think one of the main things that I want to emphasize I think that's going to be very necessary is team science. I think this is something that's absolutely critical, especially for these sorts of large-scale initiatives. When it comes to seeing science, the reality, especially when it comes to proteomics, is that an interdisciplinary team based approach is what's going to be the most valuable. No one laboratory, that's the reality, working on its own could possibly examine all the potential biomarkers, develop all of the necessary technologies for isolating and validating the biomarkers for research or clinical use, or assemble all of the pieces of evidence that's going to be required to understand the molecular mechanisms of cancer.

The bottom line, it's going to require many laboratories working together ultimately to accomplish those goals.

**Balintfy:** It's much like the Human Genome Project.

**Dr. Rodriguez:** It's very similar to the Human Genome Project, and in fact, one of the things I want to emphasize is that within that project, one of the things that allowed it to be very successful because it did involve multiple laboratories and it was an international effort, is that they helped standardize the various methodologies and the various platforms and the way the data was going to be analyzed. And proteomics is kind of falling along the same lines. It's that it's a huge area. Clearly, individual laboratories are always critical because you'll always get very good signs, but for large-scale initiatives, pulling the collectiveness together would also contribute very much to move the field forward.

**Balintfy:** And this is going to be a large-scale effort, isn't it?

**Dr. Rodriguez:** Absolutely.

**Balintfy:** Do you think after these guidelines are set up that there'll be similar achievements like there was with the Human Genome Project?

**Dr. Rodriguez:** Yes, so it's interesting. Right now, the research community is actually debating that question. So the question becomes, "Are we at a stage now where we could tackle such a large-scale effort?" I think the jury is still out, especially attributed to all the complexities that the protein world happens to bring to it versus the DNA world. I do think over time that will be something that could be obtained, but I think at the present time, what we need to do is just give ourselves the assurance that we know how to develop the proper pipelines. Once we could test that and show that we now achieve that goal, then we could start asking ourselves, what would be the next sort of initiative that could capitalize now on what we've developed in terms of this pipeline and the very robustness behind the pipeline?

**Balintfy:** Great. So in our next episode, we're going to be talking in more specifics about some of the programs that NCI is offering. So I'm looking forward to that one and thanks very much.

**Dr. Rodriguez:** You're welcome.

**Balintfy:** Dr. Henry Rodriguez at NCI. For more information about the NCI Clinical Proteomic Technologies for Cancer Initiative, visit the website [proteomics.cancer.gov](http://proteomics.cancer.gov). And be sure to tune in, in two weeks for the last of our series on proteomics. For now, that's it for this episode of NIH Research Radio. Please join us again on Friday, April 17 when our next edition will be available for download. I'm your host, Joe Balintfy. Thanks for listening.